Combat Stress or Hemorrhage? Evidence for a Decision-Assist Algorithm for Remote Triage

CAROLINE A. RICKARDS, KATHY L. RYAN, WILLIAM H. COOKE, STEVEN A. ROMERO, AND VICTOR A. CONVERTINO

RICKARDS CA, RYAN KL, COOKE WH, ROMERO SA, CONVERTINO VA. *Combat stress or hemorrhage? Evidence for a decision-assist algorithm for remote triage.* Aviat Space Environ Med 2008; 79:670–6.

Introduction: In the setting of remote military triage, when physical access to the patient is not possible, traditional physiological measurements available to a combat medic may not differentiate between a wounded soldier and an active soldier. We tested the hypothesis that changes in high-frequency R-R interval spectral power (RRI HF) and pulse pressure (PP) would differ between progressive central hypovolemia (simulated hemorrhage) and exercise to evaluate their potential for remotely distinguishing active from bleeding soldiers. The RRI HF and PP were used because of their ability to track central hypovolemia. **Methods:** There were 12 (8 female/4 male) healthy, normotensive, non-smoking subjects (age 27 ± 2 yr; height 169 ± 3 cm; weight 68 ± 5 kg) who were exposed to progressive lower body negative pressure (LBNP) and a supine cycle ergometer protocol. ECG and blood pressure were measured continuously. Exercise workloads were determined by matching the heart rate (HR) responses to each LBNP level. Data were analyzed in time and frequency domains. **Results:** HR increased from 67 ± 3 bpm at rest to 101 ± 4 bpm by −60 mmHg LBNP and was matched within 5% during exercise. By the final stage, RRI HF decreased by a similar magnitude during both LBNP (−78 ± 7%) and exercise (−85 ± 6%). PP decreased by 30 ± 4% with LBNP compared with an increase of 20 ± 6% during exercise. **Conclusion:** Monitoring PP in combination with RRI HF would distinguish a bleeding from an active soldier. Technologies that incorporate telemetry to track these derived vital signs would provide a combat medic with remote decision support to assess soldier status on the battlefield.
Keywords: heart rate variability, pulse pressure, military triage, remote monitoring.

T HE INABILITY TO triage from a remote location (physically separate from the patient) carries the risk that a combat medic may be placed in harm's way attempting to assist a soldier who may not be injured or may be unsalvageable. This risk is highlighted by data collected during the Vietnam War, indicating the fatality rate in U.S. Army medics was double that seen in other areas of the infantry (13). Anecdotally, this risk continues in the current combat setting. However, the future warfighter will likely be equipped with physiological monitoring devices that will enable continuous, remote assessment of their physical status (17,30), including an electrocardiogram (ECG) ensemble for life sign detection with the measurements of respiratory rate, heart rate (HR), R-R intervals (RRI), R-wave amplitude (24), and heart rate variability (7). In this setting, to make a remote triage decision without access to the patient, the military medic must know

if a soldier is wounded and bleeding, or simply engaged in combat.

Unfortunately, two traditionally measured vital signs, HR and respiratory rate, may not provide the specificity to differentiate between a wounded soldier and an active soldier. In contrast, high heart rate variability (i.e., variance in the time between each R-wave) is indicative of a young, healthy cardiovascular system, while a reduction in RRI variability is associated with age, disease, injury, and increased mortality (11,16,20). Measures of heart rate variability, particularly the ratio of high frequency to low frequency (HF/LF) RRI spectral power, have been proposed as potential early markers for injury severity (11,25,33) and can be associated with patient survival (10,11,34). Power spectral analysis of ECG recordings enables the assessment of relative parasympathetic and sympathetic control of the circulation (1,23,26). RRI oscillations in the high frequency (HF; 0.15–0.4 Hz) are associated primarily with parasympathetic neural control, while oscillations in the low frequency (LF; 0.04–0.15 Hz) are modulated by combined parasympathetic and sympathetic activity (1,26,34). In studies of prehospital trauma patients, a high HF/LF, representing high parasympathetic and low sympathetic predominance, was associated with mortality (10,11). Conversely, survival was indicated by a low HF/LF (i.e., low parasympathetic and high sympathetic activity) (10,11). Importantly, this index of autonomic regulation could differentiate patients who eventually lived or died when standard vital signs of HR and blood pressure (systolic, diastolic, and mean) were indistinguishable (11). These findings indicate that robust sympathetically mediated autonomic compensations to traumatic injury

Report Documentation Page		Form Approved OMB No. 0704-0188

1. REPORT DATE **01 JUL 2008**	2. REPORT TYPE **N/A**	3. DATES COVERED **-**	
4. TITLE AND SUBTITLE **Combat stress or hemorrhage? Evidence for a decision-assist algorithm for remote triage.**		5a. CONTRACT NUMBER	
		5b. GRANT NUMBER	
		5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) **Rickards C. A., Ryan K. L., Cooke W. H., Romero S. A., Convertino V. A.,**		5d. PROJECT NUMBER	
		5e. TASK NUMBER	
		5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) **United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX 78234**		8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)		10. SPONSOR/MONITOR'S ACRONYM(S)	
		11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION/AVAILABILITY STATEMENT **Approved for public release, distribution unlimited**			
13. SUPPLEMENTARY NOTES			
14. ABSTRACT			
15. SUBJECT TERMS			

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT **UU**	18. NUMBER OF PAGES **7**	19a. NAME OF RESPONSIBLE PERSON
a. REPORT **unclassified**	b. ABSTRACT **unclassified**	c. THIS PAGE **unclassified**			

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std Z39-18

are appropriate and beneficial for ultimate survival, while parasympathetic predominance reflects an inappropriate response, eventually leading to poor patient outcome (10,11,34).

In the setting of controlled central hypovolemia induced by application of lower body negative pressure (LBNP) in conscious humans, decreases in RRI HF track the withdrawal of parasympathetic activity with the progressive reduction in central blood volume (7,8,14,21). Since the RRI HF inversely tracks the increase in muscle sympathetic nerve activity (8) and decreases well in advance of changes in mean arterial blood pressure (7) during central hypovolemia, continuous measurement of the RRI HF in a remote triage setting could indicate the severity and progression of hemorrhagic injury and highlight the requirement for life saving interventions earlier than standard vital signs. Unfortunately, the reduction of RRI HF under other physiological conditions that elicit sympathetic activation and parasympathetic withdrawal such as exercise (2,27,35), heat stress (3,12), dehydration, and psychological stress (15), could interfere with the interpretation of a decreasing RRI HF as an indicator of a bleeding casualty. To reduce the potential for combat medics placing themselves in unnecessary life threatening situations, it is therefore essential to know whether a low RRI HF is associated with a survivable injury requiring medical attention or simply an active soldier in the midst of a physically demanding confrontation.

To achieve this objective, it is highly likely that more than one physiological measurement will be required. Pulse pressure (PP, i.e., systolic minus diastolic blood pressure) is a potential index for this purpose, as it may provide early differentiation between trauma patients who can survive or will die from their injuries (10), and it also tracks the reduction of central blood volume during LBNP (4) and the increase in central blood volume during exercise (28). As such, traditionally measured blood pressures (i.e., systolic and diastolic) could provide a novel index of blood volume changes via the simple calculation of PP.

This study was designed to evaluate the potential utility of both the RRI HF and PP in differentiating a bleeding soldier from an active soldier with remote monitoring technology. While the RRI HF is known to decrease under both conditions, and pulse pressure tracks the divergent alterations in central blood volume, the temporal pattern and magnitude of these responses are not known. We tested the hypothesis that the reductions in RRI HF in combination with lower PP would differentiate central hypovolemia (simulated hemorrhage) from RRI HF and PP responses induced by exercise in the setting of remote military triage.

METHODS

Subjects

There were 12 (8 female, 4 male) healthy, normotensive, nonsmoking subjects who volunteered to participate in this study (age 27 ± 2 yr; height 169 ± 3 cm;

weight 68 ± 5 kg), conducted at the U.S. Army Institute of Surgical Research, Fort Sam Houston, TX, and the University of Texas at San Antonio, San Antonio, TX. All experimental procedures and protocols were reviewed and approved by the Institutional Review Boards of the Brooke Army Medical Center, Fort Sam Houston, TX, and the University of Texas at San Antonio. A complete medical history and physical examination was obtained on each of the potential subjects prior to being approved for testing. In addition, female subjects underwent a urine pregnancy test within 24 h of experimentation for the LBNP portion of the study, and were excluded from participation if pregnant. Subjects were instructed to maintain their normal sleep pattern and refrain from exercise, alcohol, and stimulants such as caffeine and other nonprescription drugs 24 h prior to testing in order to reduce their potential acute effects on cardiovascular responsiveness. During a familiarization session that preceded each experiment, subjects received a verbal briefing and a written description of all procedures and risks associated with the experiments, and were made familiar with the laboratory, the protocol, and procedures. Each subject gave their written informed consent to participate in the study.

Study Design

In order to test the hypothesis, each subject was required to undergo exposure to a progressive LBNP protocol and a graded exercise protocol. The LBNP protocol was performed first so that exercise workloads could be chosen that reproduced the HR response generated by the LBNP. LBNP was used as an experimental tool to reduce central blood volume (e.g., simulated hemorrhage) (9). With the use of a neoprene skirt designed to form an airtight seal between the subject and the chamber, the application of negative pressure to the lower body (below the iliac crest) results in a redistribution of blood away from the upper body (head and heart) to the abdomen and lower extremities. Thus, this technique provides a unique model of controlled, experimentally induced hypovolemic hypotension.

All subjects were instrumented for noninvasive, continuous measurements of HR (standard lead II ECG), and beat-to-beat arterial blood pressures (Finometer® infrared finger plethysmography, TNO-TPD Biomedical Instrumentation, Amsterdam, The Netherlands). An appropriately sized Finometer® blood pressure cuff was placed on the middle finger of the left hand. Respiratory rate was measured breath-by-breath at the mouth using an infrared end tidal CO_2 sensor (Gambro, Entröm, Sweden) attached to a facemask.

Each subject was exposed to a LBNP protocol designed to test their tolerance to experimentally induced hypotensive hypovolemia. The LBNP protocol consisted of a 5-min rest period (baseline) followed by 5 min of chamber decompression to −15, −30, −45, and −60 mmHg, and additional increments of −10 mmHg every 5 min until the onset of cardiovascular collapse or the completion of 5 min at −100 mmHg. Cardiovascular

collapse was defined by one or a combination of the following criteria: 1) sudden bradycardia; 2) a precipitous fall in systolic blood pressure (SBP) greater than 15 mmHg; 3) progressive diminution of SBP below 70 mmHg; or, 4) voluntary subject termination due to the onset of presyncopal symptoms such as gray-out, sweating, nausea, dizziness, or general discomfort. The final 3 min of each 5-min LBNP level was used for data analysis to ensure stable recordings.

With at least 4 d intervening, subjects completed the exercise portion of the study, consisting of a supine cycle ergometer protocol. A supine cycle ergometer was chosen as the mode of exercise in an effort to match body position during exercise with that during central hypvolemia. Arterial blood pressure, HR, and respiratory rate were recorded continuously using the same techniques as the LBNP trial. The exercise protocol consisted of a 5-min baseline followed by 5-min levels of exercise at progressively increasing workloads. Each exercise workload was determined by matching the HR response to each LBNP level. For example, if HR was 70 bpm during the final 3 min of −15 mmHg LBNP, the first exercise workload was adjusted to elicit a HR of 70 bpm. As HR increases with both LBNP and exercise, HRs were matched to ensure any differences in the measurement of heart rate variability were due to the condition (LBNP or exercise) rather than a difference in absolute HR response. The total number of exercise workloads was determined by the total number of completed LBNP levels. The first 2 min of each exercise level were used to stabilize HRs at the desired level while the final 3 min were used for data analysis.

Data Analysis

Continuous, beat-to-beat ECG and blood pressure waveforms, and breath-to-breath respiratory (etco$_2$) waveforms were sampled at 500 Hz and recorded directly to a computer-based data acquisition software package (WinDAQ, Dataq Instruments, Akron, OH), then exported and analyzed with commercially available analysis software (WinCPRS, Absolute Aliens, Turku, Finland). R waves generated from the ECG signal were detected and marked at their occurrence in time. Diastolic blood pressure (DBP) and SBP were subsequently marked from the Finometer® tracings. PP was calculated by subtracting DBP from SBP. Respiratory rate (breaths/min) was calculated from the peaks of the $P_{et}CO_2$ waveform.

Heart rate variability was assessed in the frequency domain from R-R interval spectral power. To calculate spectral power, consecutive RRIs were replotted using linear interpolation and resampled at 5 Hz. Data were then passed through a low-pass impulse response filter with a cutoff frequency of 0.5 Hz. To obtain power spectra, 3-min data sets were fast Fourier transformed with a Hanning window. Spectral power was expressed as the integrated area within the HF (0.15–0.4 Hz) range. The final 3 min of each LBNP level and exercise level were used for statistical comparison of time and frequency domain variables between the two conditions.

Statistical Analysis

A repeated measures 2-way analysis of variance was used to compare the cardiovascular responses to LBNP and exercise (condition factor) at each level (time factor), followed by Tukey post hoc tests. All data are presented as mean ± SE and exact P-values are presented for all comparisons (22).

RESULTS

As the LBNP protocol was terminated upon the presence of presyncopal symptoms, tolerance time for each subject was variable. However, as all 12 subjects reached the LBNP level of −60 mmHg (baseline plus four stages), we compared the cardiovascular responses over four stages of LBNP with the HR-matched four stages of exercise. Baseline values for all variables of interest under both the LBNP and exercise conditions are presented in **Table I**.

HR increased from 67 ± 4 bpm to 101 ± 4 bpm by −60 mmHg LBNP ($P < 0.001$). For each level of exercise, HR was successfully matched within 5% of LBNP measurements, from 65 ± 3 bpm at baseline to 102 ± 5 bpm at the final exercise stage. RRI HF decreased from baseline to stage 4 during both LBNP (−78 ± 7%, $P = 0.058$) and exercise (−85 ± 6%, $P < 0.001$). It was not possible to differentiate either the HR (**Fig. 1A**) or RRI HF (**Fig. 1B**) responses between the two conditions at any stage of LBNP and exercise ($P \geq 0.184$). PP responses diverged with progressive LBNP and exercise (**Fig. 2**). By the final stage of LBNP, PP decreased by 30 ± 4% ($P < 0.001$) compared with an increase of 20 ± 6% ($P < 0.001$) during exercise. SBP increased progressively during exercise and decreased during LBNP, with differences detected between the two conditions by stage 3 (**Fig. 3A**). Respiratory rate did not change during LBNP, but increased immediately upon the onset of exercise ($P < 0.001$), reaching a maximum of 21 ± 1 breaths/min (**Fig. 3B**).

DISCUSSION

Our previous analyses of ECG data obtained from severely injured trauma patients revealed that an elevated HF/LF distinguished survivors from non-survivors many hours prior to changes in standard vital signs such as SBP, HR, and arterial oxygen saturation (10,11). Although an elevated HF/LF (i.e., parasympathetic

TABLE I. BASELINE VALUES FOR THE LBNP AND EXERCISE CONDITIONS (MEANS ± SE).

Variable	LBNP	Exercise	P-Value
Heart Rate, bpm	67 ± 3	65 ± 3	0.204
Systolic Blood Pressure, mmHg	132 ± 3	127 ± 3	0.268
Respiratory rate, breaths/min	15 ± 1	15 ± 1	0.659
Pulse Pressure, mmHg	54 ± 3	62 ± 3	0.017
RRI HF, ms^2	1495 ± 455	2390 ± 693	0.184

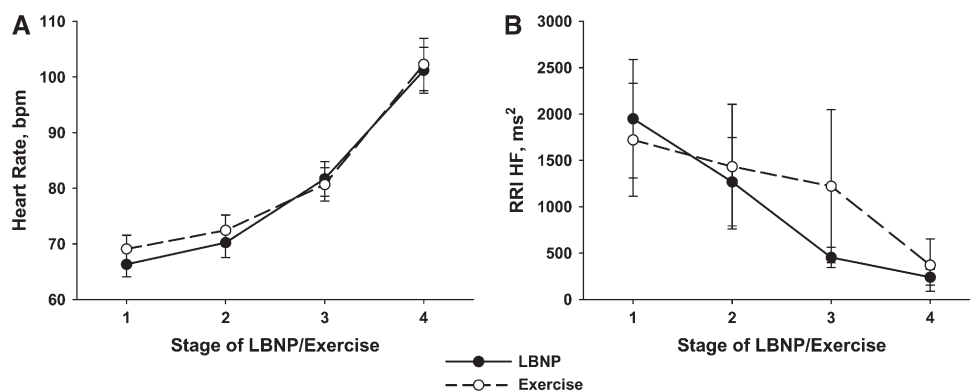LBNP = lower-body negative pressure; RRI HF = high frequency RRI variability.

Fig. 1. A) Heart rate and B) RRI HF responses to four stages of lower body negative pressure (LBNP) up to −60 mmHg (solid line, black circles) and four stages of HR-matched exercise (dashed line, open circles).

predominance) might represent a sensitive marker of eventual mortality in a combat trauma scenario, detection of reduced parasympathetic activity (RRI HF) under these conditions could indicate either early, appropriate, autonomic compensation to hemorrhage or a healthy, uninjured soldier actively moving to a safe position. The ability to differentiate between these two conditions of elevated sympathetic and reduced parasympathetic activity is essential for appropriate and effective treatment decisions in a remote triage setting, i.e., where the patient is not physically accessible.

We, therefore, hypothesized that the magnitude of changes in the RRI HF during progressive central hypovolemia could differ from changes during exercise, enabling the differentiation of these two conditions based on heart rate variability analyses. Contrary to our hypothesis, we demonstrated that the RRI HF decreased in a similar fashion with both progressive central hypovolemia and during mild graded exercise when HR responses were similar. These findings clearly highlight that indices of heart rate variability alone will not be sufficient to distinguish a physically active soldier from a bleeding soldier when autonomic mechanisms are adequately compensating for loss of blood, particularly if the medic does not have visual or verbal contact with

the soldier. Thus, our findings provide evidence that the measurements of other physiological responses are required in addition to heart rate variability to accurately identify the physiological condition of combat casualties in a remote triage setting.

With our experimental approach, we were able to identify that the addition of PP measurements can distinguish between physical activity and the reduction in central blood volume from an early stage. This is not unexpected since PP tracks changes in central blood volume and stroke volume (4), which increase with exercise (18) and decrease with LBNP (9). These measurements that we are proposing to enhance the capabilities of monitoring casualties will improve and/or replace those vital signs that currently represent the standard of care. In studies of severely injured trauma patients in the pre-hospital setting, the HF/LF and PP separated survivors from non-survivors when the standard vital signs of HR, SBP, and arterial oxygen saturation were indistinguishable (10,11). Furthermore, in laboratory studies where the physiological responses of hemorrhage can be simulated by progressive reductions in central blood volume, RRI HF and PP start to change from an early stage (4,7) while SBP (4), arterial oxygen saturation (5), and pulse character (29) remain relatively stable. As such, current vital signs either lack the sensitivity to be early indicators of physiological deterioration, and change only when it may be too late for interventions to be effective, or are not specific to distinguish between conditions of injury and activity for use in the remote triage setting. The proposed measure of RRI HF is sensitive while PP is both sensitive and specific, so together these indices would provide valuable information to advance the capabilities of the combat medic.

The development of a remote triage capability for combat medics has important life-saving implications. In the current combat setting, medics routinely place themselves in an unprotected, potentially vulnerable position in order to physically assess a soldier for diagnosis of mode and severity of injury, initiation of treatment, and prioritization of evacuation. In some cases, however, a medic will attend to a soldier who is either uninjured but caught in the vicinity of the combat, or a soldier who has injuries that are deemed unsalvageable. The high mortality rate of combat medics is best sup-
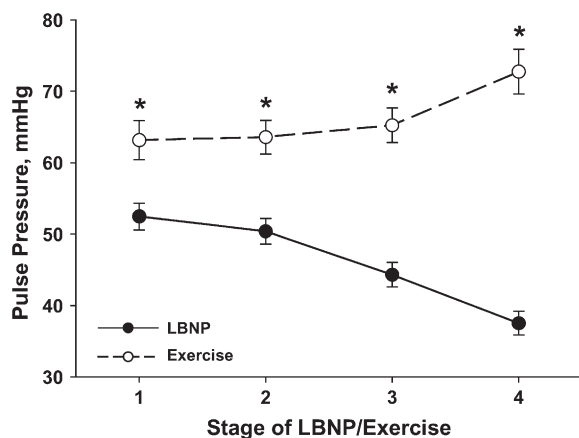

Fig. 2. Pulse pressure response to four stages of LBNP up to −60 mmHg (solid line, black circles) and four stages of exercise (dashed line, open circles). Asterisk (*) designates $P \leq 0.002$ between the LBNP and exercise conditions at that stage.
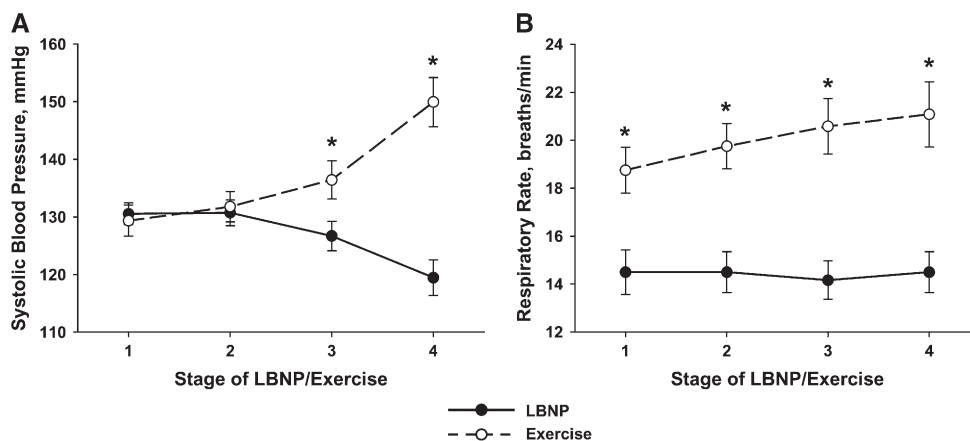
Fig. 3. A) Systolic blood pressure and B) respiratory rate responses to four stages of LBNP up to −60 mmHg (solid line, black circles) and exercise (dashed line, open circles). Asterisk (*) designates $P \leq 0.023$ between the LBNP and exercise conditions at that stage.

ported by data collected in Vietnam and retrieved from the Combat Area Casualty File of the National Archives (13). Of the 58,169 U.S. personnel killed in action (KIA) in Vietnam, U.S. Army infantryman KIA totaled 20,460. With full unit strength, there was 1 medic assigned to every 31 infantryman. Given normal distribution of KIA, the medics should have had a KIA rate of 3.2% of the total infantry, or an estimated 660 medics. However, the actual Army medic KIA in Vietnam was 6.6% (1342 medics), more than double the expected rate. Furthermore, it is highly likely that a significant proportion of these medics were attending casualties who had suffered nonsurvivable injuries. The ability to remotely monitor the physiological status of soldiers from a protected location would reduce unnecessary risk of injury and enable the medic to safely and accurately triage and attend to only those soldiers requiring immediate medical care.

Our findings highlight the unlikely scenario that a single measure will be sufficient to adequately assess the physiological status of casualties and make appropriate treatment decisions. Rather, a series of input signals obtained from the soldier will be required to advance a robust decision-assist algorithm (**Fig. 4**). To facilitate remote physiological monitoring, the future warfighter will be equipped with devices that will enable the continuous assessment of their physiological condition with such measurements as ballistic impact, core body temperature, body orientation and movement, respiration, and HR (17,30). Our data suggest that the capabilities of combat medics to perform remote triage will be significantly advanced with the development of a sensor system that also provides noninvasive, continuous measurement, calculation, and integration of both heart rate variability (i.e., RRI HF) and PP.

In a combat situation where a medic is remotely monitoring a solider who has registered a ballistic impact, determining whether the soldier is severely wounded and hemorrhaging or uninjured and engaging in a physically demanding activity could be achieved via a series of sequential decision-support steps. First, the technical functionality of the monitoring equipment would need to be confirmed (i.e., accurately and reliably measuring all variables). If a problem is detected, an error signal would display and the system could not be used further

for decision assist. HR and RRI HF would then be detected and calculated via an ECG, providing information on autonomic compensatory reflexes. A decreasing RRI HF will indicate that the solider is compensating appropriately either from an injury or from physical activity. The measurement of PP will distinguish between these two conditions: a soldier with a decreasing RRI HF and increasing PP is most likely uninjured and physically active, so no intervention is required, while a soldier with a decreasing RRI HF and decreasing PP is most likely injured, bleeding, and requires immediate medical attention, and evacuation procedures should be initiated. Conversely, an increasing RRI HF with a known ballistic impact may be indicative of parasympathetic predominance, and in combination with a decreasing PP suggests the soldier is bleeding and decompensating, so in immediate need of medical attention and evacuation to a higher echelon of care. However, the combination of increasing RRI HF and decreasing PP is also consistent with an uninjured soldier who may be relaxing following physical exertion. Adjunct inputs to this decision-assist algorithm include a respiration signal, body movement and position (provided by an accelerometer or global positioning system), and verbal and motor responses to a radio command [similar functions to the verbal and motor components of the Glasgow Coma Score (31,32)] incorporated into the monitoring system (i.e., a "911" call). These measures will enable the distinction between an active and bleeding soldier under these conditions. These additional measurements in combination with the HR signal are also essential in determining whether a soldier is expectant, with a low priority for medical attention and evacuation. All four physiological criteria would need to be met for this classification.

Importantly, the measurements of HR, RRI HF, and PP would be continuous to enable trending of these responses, which is more sensitive and accurate than a single static measure as indicated in Fig. 1–3. Trending is particularly relevant to RRI HF measurements due to high intra- and interindividual variability in this metric, even under identical physiological conditions (e.g., baseline RRI HF in Table I). As such, in a combat scenario where multiple soldiers are being monitored
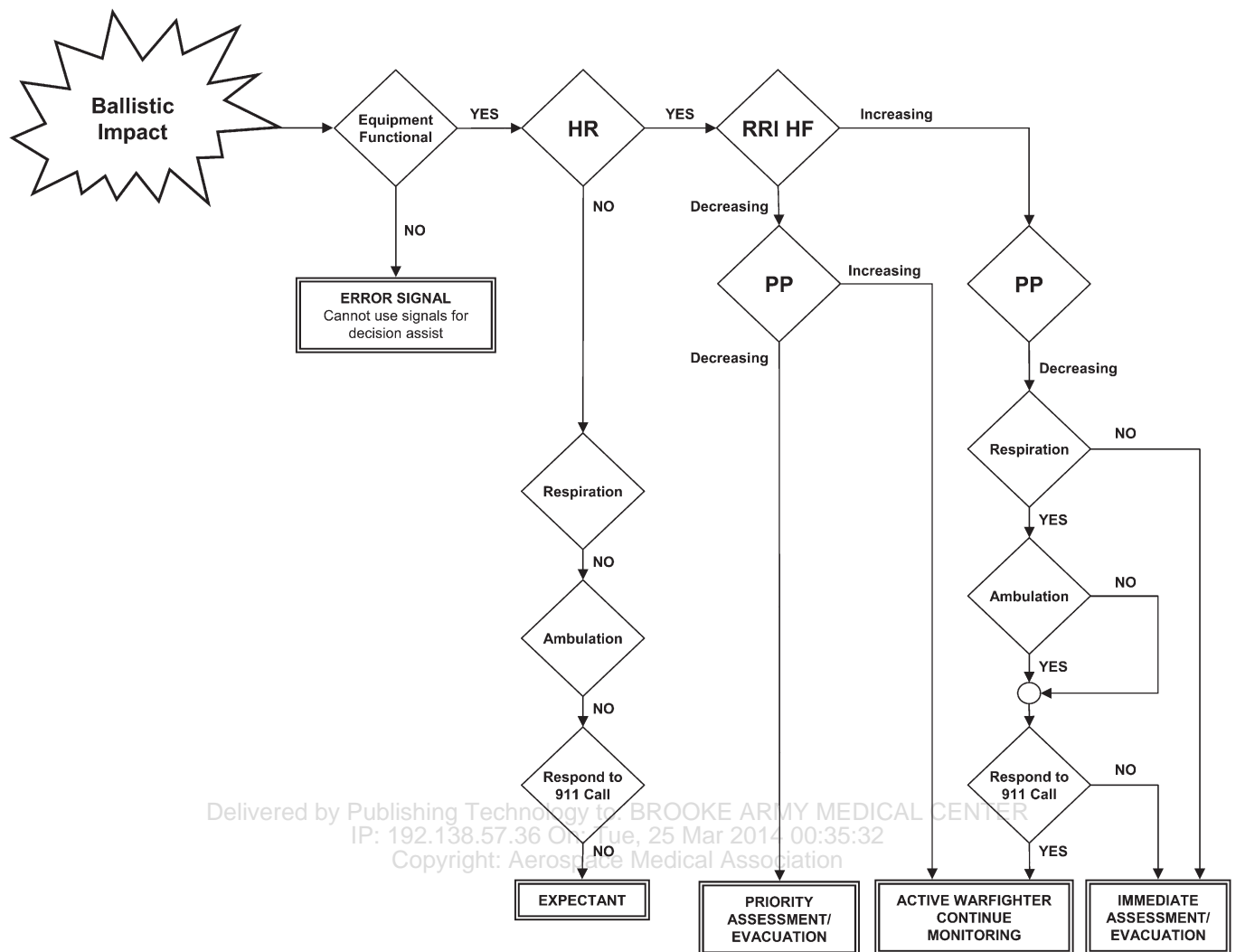
Fig. 4. Schematic representation of a decision-assist algorithm for the triage of military casualties into one of four categories: injured and decompensating, requiring immediate, high priority evacuation; injured and compensating appropriately, requiring priority evacuation; not injured, no evacuation required; or, expectant, requiring very low priority evacuation. HR, heart rate; RRI HF, high-frequency RRI variability; PP, pulse pressure.

simultaneously, single "snap-shot" measurements of RRI HF or PP will not distinguish the physiological condition of soldiers; this can only be achieved by monitoring the progress of cardiovascular compensation (to injury or activity) over time.

Physiological monitoring without physical access to the patient has inherent limitations. It is possible that additional autonomic stimuli (e.g., beta blockers, caffeine, dehydration, hypothermia, nerve gas) could influence the RRI HF and/or PP beyond the effect of the hemorrhage or physical activity, generating false positives or false negatives. However, the inclusion of multiple physical and physiological inputs into this decision assist algorithm should provide the combat medic with information that suggests a scenario consistent with injury (i.e., ballistic impact, no ambulation, no response to verbal command, and a decreasing RRI HF and PP). These levels of redundancy should reduce the potential for the decision-assist algorithm to generate false positive or false negative results.

While the purpose of this study is primarily focused on the application of the decision-assist algorithm to the remote triage environment, physiological markers that track changes in volume status would also be valuable in higher echelons of medical care. For example, tracking PP and RRI HF could indicate: 1) whether bleeding has been controlled; 2) the progress of fluid resuscitation therapy; and 3) rebleeding and decompensation if fluid resuscitation has dislodged a clot. As important, a capability of continuous RRI HF and PP measurements added to standard medical monitors could provide needed autonomous care (e.g., closed loop resuscitation) during transport of combat casualties (6,19). Thus, the simple combination of PP and RRI HF measurements could provide a more sensitive indicator of volume status than standard vital signs, e.g., radial pulse, SBP, and arterial oxygen saturation.

This study clearly demonstrates that the RRI HF spectral power alone would not differentiate bleeding soldiers from active soldiers in a remote triage setting. However, with additional, complementary information such as

PP and ambulation status, the RRI HF may prove useful in the setting of military triage in determining the severity of a soldier's medical condition following a wounding event, and the requirement for immediate attention. At present, the measurement of PP or a surrogate of PP cannot be obtained remotely with currently available monitoring devices. The results of our investigation highlight the need to advance the development of such devices to ensure that the most sensitive and specific indices of injury status and progression are measured in the remote triage setting. Our data are the first to suggest that RRI HF and PP could be important adjuncts to standard vital signs and/or indicators of activity status in advancing the remote triage capabilities of combat medics.

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